

WHAT IS CLAIMED IS:

1 1. A method for treating cancer comprising administering to a subject in
2 need of such treatment a therapeutically effective amount of

3 (a) a member selected from an inhibitor of a protein kinase, an enantiomer of
4 such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such
5 a compound, and combinations thereof; and

6 (b) an agent that inhibits a cellular ATP synthetic pathway.

1 2. The method of claim 1, wherein the agent that inhibits a cellular ATP
2 synthetic pathway is a member selected from an inhibitor of inosine monophosphate
3 dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound,
4 a pharmaceutically acceptable salt of such a compound, and combinations thereof.

1 3. The method of claim 2, wherein the IMPDH inhibitor is selected from
2 the group consisting of mizoribine, mizoribine aglycone, mycophenolate mofetil, tiazofurin,
3 viramidine, and ribavarin.

1 4. The method of claim 2, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 5. The method of claim 4, wherein the inhibitor of the receptor tyrosine
2 kinase is Gleevec.

1 6. The method of claim 5, wherein the receptor tyrosine kinase is selected
2 from the group consisting of Bcr-Abl, Abl, PDGFR, and c-kit.

1 7. The method of claim 5, wherein the receptor tyrosine kinase is Bcr-Abl
2 and the cancer is chronic myelogenous leukemia.

1 8. The method of claim 5, wherein the receptor tyrosine kinase is c-kit
2 and the cancer is gastrointestinal stromal tumor.

1 9. The method of claim 4, wherein the inhibitor of the receptor tyrosine
2 kinase is selected from the group consisting of AD1839 (Iressa), OSI-774, PKI116, GW2016,
3 EKB-569, and CI1033.

1 10. The method of claim 9, wherein the receptor tyrosine kinase is selected
2 from the group consisting of ErbB1, ErbB2, ErbB3, and ErbB4.

1 11. The method of claim 9, wherein the inhibitor of the receptor tyrosine
2 kinase is AD1839 (Iressa).

1 12. The method of claim 9, wherein the cancer is selected from the group
2 consisting of non-small-cell lung cancer, squamous cell carcinoma of the head and neck, and
3 hormone refractory prostate cancer.

1 13. The method of claim 2, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 14. The method of claim 13, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 15. A composition for treating cancer in a subject in need of such
2 treatment comprising therapeutically effective amounts of
3 (a) a member selected from an inhibitor of a protein kinase, an enantiomer of
4 such a compound, a prodrug of such a compound, a pharmaceutically acceptable salt of such
5 a compound, and combinations thereof; and
6 (b) an agent that inhibits a cellular ATP synthetic pathway.

1 16. The composition of claim 15, wherein the agent that inhibits a cellular
2 ATP synthetic pathway is a member selected from an inhibitor of inosine monophosphate
3 dehydrogenase (IMPDH), an enantiomer of such a compound, a prodrug of such a compound,
4 a pharmaceutically acceptable salt of such a compound, and combinations thereof.

1 17. The composition of claim 16, wherein the IMPDH inhibitor is selected
2 from the group consisting of mizoribine, mizoribine aglycone, mycophenolate mofetil,
3 tiazofurin, viramidine, and ribavarin.

1 18. The composition of claim 16, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 19. The composition of claim 18, wherein the receptor tyrosine kinase
2 inhibitor is selected from the group consisting of Gleevec, AD1839 (Iressa), OSI-774,
3 PKI116, GW2016, EKB-569, and CI1033.

1 20. The composition of claim 16, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 21. The composition of claim 20, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 22. The method of claim 1, wherein the agent that inhibits a cellular ATP
2 synthetic pathway is a member selected from an inhibitor of the *de novo* pathway of purine
3 biosynthesis, a prodrug therefor, or a pharmaceutically acceptable salt thereof, and
4 combinations thereof.

1 23. The method of claim 22, wherein the inhibitor of the *de novo* pathway
2 of purine biosynthesis is selected from the group consisting of L-alanosine, methotrexate,
3 trimetrexate, 10-propargyl-5,8-dideazafolic acid (PDDF), *N*-[5-[*N*-(3,4-dihydro-2-methyl-4-
4 oxoquinazolin-6-ylmethyl)-*N*-methylamino]-2-thenoyl]-L-glutamic acid (ZD1694, Tomudex),
5 *N*-[4-[2-(2-amino-3,4-dihydro-4-oxo-7*H*-pyrrolo[2,3-*d*]-pyrimidin-5-yl)ethyl]-benzoyl]-L-
6 glutamic acid (LY231514), 6-(2'-formyl-2'naphthyl-ethyl)-2-amino-4(3*H*)-oxoquinazoline
7 (LL95509), (6*R,S*)-5,10-dideazatetrahydrofolic acid (DDATHF), 4-[2-(2-amino-4-oxo-
8 4,6,7,8-tetrahydro-3*H*pyrimidino[5,4,6][1,4]-thiazin-6yl)-(S)-ethyl]-2,5-thienoylamino-L-
9 glutamic acid (AG2034), and *N*-[5-(2-[(2,6-diamino-4(3*H*)-oxopyrimidin-5-
10 yl)thio]ethyl)thieno-2-yl]-L-glutamic acid (AG2009).

1 24. The method of claim 22, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 25. The method of claim 24, wherein the inhibitor of the receptor tyrosine
2 kinase is Gleevec.

1 26. The method of claim 25, wherein the receptor tyrosine kinase is
2 selected from the group consisting of Bcr-Abl, Abl, PDGFR, and c-kit.

1 27. The method of claim 25, wherein the receptor tyrosine kinase is Bcr-
2 Abl and the cancer is chronic myelogenous leukemia.

1 28. The method of claim 25, wherein the receptor tyrosine kinase is c-kit
2 and the cancer is gastrointestinal stromal tumor.

1 29. The method of claim 24, wherein the inhibitor of the receptor tyrosine
2 kinase is selected from the group consisting of AD1839 (Iressa), OSI-774, PKI116, GW2016,
3 EKB-569, and CI1033.

1 30. The method of claim 29, wherein the receptor tyrosine kinase is
2 selected from the group consisting of ErbB1, ErbB2, ErbB3, and ErbB4.

1 31. The method of claim 29, wherein the inhibitor of the receptor tyrosine
2 kinase is AD1839 (Iressa).

1 32. The method of claim 29, wherein the cancer is selected from the group
2 consisting of non-small-cell lung cancer, squamous cell carcinoma of the head and neck, and
3 hormone refractory prostate cancer.

1 33. The method of claim 22, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 34. The method of claim 33, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,

3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 35. The method of claim 22, wherein the cancer comprises a population of
2 cells deficient in the enzyme methyladenosine phosphorylase (MTAP).

1 36. A method for treating cancer in a subject in need of such treatment,
2 wherein the cancer comprises of a population of cells deficient in the enzyme
3 methyladenosine phosphorylase (MTAP), comprising:

4 administering to the subject a therapeutically effective amount of a member
5 selected from an inhibitor of a protein kinase, an enantiomer of such a compound, a prodrug
6 of such a compound, a pharmaceutically acceptable salt of such a compound, and
7 combinations thereof.

1 37. The method of claim 36, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 38. The method of claim 37, wherein the receptor tyrosine kinase inhibitor
2 is selected from the group consisting of Gleevec, AD1839 (Iressa), OSI-774, PKI116,
3 GW2016, EKB-569, and CI1033.

1 39. The method of claim 36, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 40. The method of claim 39, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 41. The composition of claim 15, wherein the agent that inhibits a cellular
2 ATP synthetic pathway is a member selected from an inhibitor of the *de novo* pathway of
3 purine biosynthesis, a prodrug therefor, or a pharmaceutically acceptable salt thereof, and
4 combinations thereof.

1 42. The composition of claim 41, wherein the inhibitor of the *de novo*
2 pathway of purine biosynthesis is selected from the group consisting of L-alanosine,
3 methotrexate, trimetrexate, 10-propargyl-5,8-dideazafolic acid (PDDF), *N*-[5-[*N*-(3,4-
4 dihydro-2-methyl-4-oxoquinazolin-6-ylmethyl)-*N*-methylamino]-2-thenoyl]-L-glutamic acid
5 (ZD1694, Tomudex), *N*-[4-[2-(2-amino-3,4-dihydro-4-oxo-7*H*-pyrrolo[2,3-*d*]-pyrimidin-5-
6 yl)ethyl]-benzoyl]-L-glutamic acid (LY231514), 6-(2'-formyl-2'naphthyl-ethyl)-2-amino-
7 4(3*H*)-oxoquinazoline (LL95509), (6*R,S*)-5,10-dideazatetrahydrofolic acid (DDATHF), 4-[2-
8 (2-amino-4-oxo-4,6,7,8-tetrahydro-3*H*pyrimidino[5,4,6][1,4]-thiazin-6yl)-(S)-ethyl]-2,5-
9 thienoylamino-L-glutamic acid (AG2034), and *N*-[5-(2-[(2,6-diamino-4(3*H*)-oxopyrimidin-5-
10 yl)thio]ethyl)thieno-2-yl]-L-glutamic acid (AG2009).

1 43. The composition of claim 41, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 44. The composition of claim 43, wherein the receptor tyrosine kinase
2 inhibitor is selected from the group consisting of Gleevec, AD1839 (Iressa), OSI-774,
3 PKI116, GW2016, EKB-569, and CI1033.

1 45. The composition of claim 41, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 46. The composition of claim 45, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 47. The method of claim 1, wherein the agent that inhibits a cellular ATP
2 synthetic pathway is a member selected from an inhibitor of the salvage pathway of ATP
3 biosynthesis, a prodrug therefor, or a pharmaceutically acceptable salt thereof, and
4 combinations thereof.

1 48. The method of claim 47, wherein the inhibitor of the salvage pathway
2 of ATP biosynthesis is selected from the group consisting of N7-((1'R,2'S,3'R,4'S)-2',3'-

3 dihydroxy-4'-amino-cyclopentyl)-4-amino-5-bromo-pyrrolo[2,3-a]pyrimidine , 5'-
4 aminotubercidin, 5-amino-5'-deoxyadenosine, 5'-deoxy-5'-amino-clitocine, 4-amino-5-(3-
5 bromophenyl)-7-(6-morpholino-pyridin-3-yl)pyrido[2,3-d]pyrimidine, 5-iodotubercidin (5-
6 IT), and 5'-deoxy,5-iodotubercidin (5'd-5IT).

1 49. The method of claim 47, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 50. The method of claim 49, wherein the receptor tyrosine kinase inhibitor
2 is selected from the group consisting of Gleevec, AD1839 (Iressa), OSI-774, PKI116,
3 GW2016, EKB-569, and CI1033.

1 51. The method of claim 47, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 52. The method of claim 51, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.

1 53. The composition of claim 15, wherein the agent that inhibits a cellular
2 ATP synthetic pathway is a member selected from an inhibitor of the salvage pathway of
3 ATP biosynthesis, a prodrug therefor, or a pharmaceutically acceptable salt thereof, and
4 combinations thereof.

1 54. The composition of claim 53, wherein the inhibitor of the salvage
2 pathway of ATP biosynthesis is selected from the group consisting of N7-((1'R,2'S,3'R,4'S)-
3 2',3'-dihydroxy-4'-amino-cyclopentyl)-4-amino-5-bromo-pyrrolo[2,3-a]pyrimidine , 5'-
4 aminotubercidin, 5-amino-5'-deoxyadenosine, 5'-deoxy-5'-amino-clitocine, 4-amino-5-(3-
5 bromophenyl)-7-(6-morpholino-pyridin-3-yl)pyrido[2,3-d]pyrimidine, 5-iodotubercidin (5-
6 IT), and 5'-deoxy,5-iodotubercidin (5'd-5IT).

1 55. The composition of claim 53, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a receptor tyrosine kinase, a prodrug therefor, a
3 pharmaceutically acceptable salt thereof, and combinations thereof.

1 56. The composition of claim 55, wherein the receptor tyrosine kinase
2 inhibitor is selected from the group consisting of Gleevec, AD1839 (Iressa), OSI-774,
3 PKI116, GW2016, EKB-569, and CI1033.

1 57. The composition of claim 53, wherein the protein kinase inhibitor is a
2 member selected from an inhibitor of a serine kinase, a prodrug therefor, a pharmaceutically
3 acceptable salt thereof, and combinations thereof.

1 58. The composition of claim 57, wherein the inhibitor of a serine kinase is
2 selected from the group consisting of isopentenyladenine, 6-dimethylaminopurine,
3 olomoucine, roscovitine, CVT-313, purvanol, butyrolactone-I, flavopiridols, staurosporine,
4 indirubins, hymenialdesine, and paullones.